Surgical Management of Keratoconus
Jim Owen, OD MBA, FAAO

Financial Disclosure
• Jim Owen, OD has no financial interests in any of the products or companies discussed in this program

Keratoconus
Asymmetric, bilateral progressive, thinning disorder of the cornea

Keratoconus
• Adolescent onset
• Progresses over 10-20 years
• Prevalence: 50-230/100,000\(^1\)
• Incidence
  • 1/5000 in general population\(^2\)
  • 2% in patients seeking surgical correction of refractive errors\(^3\)
• About 10% of patients with KC require corneal transplantation

Penetrating Keratoplasty

How Many PKP’s Occur in the United States Secondary to Keratoconus?
1. 500
2. 2250
3. 5000
4. 7500
Who is not at Risk

Spoerl et al., J Refractive Surg. 2008:24:7:

Percentage of Smokers and Nonsmokers in Average German Population and Patients With Keratoconus

<table>
<thead>
<tr>
<th></th>
<th>Average Population</th>
<th>Keratoconus</th>
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<tbody>
<tr>
<td>Smokers</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>Non-Smokers</td>
<td>70</td>
<td>95</td>
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Methods Of Stiffening the Cornea

- Glutaraldehyde crosslinking (prosthetic heart valves)
- Formaldehyde (pathology specimens)
- Aldehyde sugars (diabetes)
- UVA-induced crosslinking (dentistry)

Riboflavin Absorption Spectrum

Collegen Cross-Linking History

- Studied since 1994
  - University of Dresden
  - Theo Seiler
  - Eberhard Spoerl
  - Gregory Wollensak

III International Congress of Corneal Cross-linking

- Abbreviations in literature confusing
  - CCC
  - C3R
  - CCL
- Universal standard going forward - CXL
1. Riboflavin (vit. B2) + Ultraviolet radiation

2. Production of oxygen radicals (ROS)

3. Induction of collagen cross-links

UVA Corneal Absorption in Presence of Riboflavin

<table>
<thead>
<tr>
<th>Irradiance</th>
<th>Damage Threshold</th>
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<tbody>
<tr>
<td>3.00 mW/cm²</td>
<td>Keratocytes: 0.5 mW/cm²</td>
</tr>
<tr>
<td>1.49 mW/cm²</td>
<td>Endothelium: 0.3 mW/cm²</td>
</tr>
<tr>
<td>0.74 mW/cm²</td>
<td></td>
</tr>
<tr>
<td>0.36 mW/cm²</td>
<td></td>
</tr>
<tr>
<td>0.18 mW/cm²</td>
<td></td>
</tr>
<tr>
<td>0.09 mW/cm²</td>
<td></td>
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<tr>
<td>0.06 mW/cm²</td>
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Effect of Corneal Cross-Linking

Riboflavin + UVA Effect

Anterior View

Posterior View

Riboflavin + UVA vs. Riboflavin alone, 30min treatment

Asota, Fant, Edelhauser, and Stulting, unpublished

Confocal Micrograph at 300 microns

Pretreatment

30 Days Post Treatment

Riboflavin/UV Cross-Linking
Pachymetry

Riboflavin 0.1% q 2 minutes/30 minutes

Fluorescence in Anterior Chamber

Riboflavin q 2 minutes and UV Light for 30 minutes

UV Light for 30 Minutes

Bandage Contact Lens
Which step in this treatment gives you the most anxiety?

1. Removing epithelium
2. Applying Riboflavin
3. Exposing eye to UV Light
4. Applying Bandage Contact Lens
5. Watching Epithelium Grow

Epithelial-On Crosslinking (Transepithelial CXL)

- First performed by Brian Boxer Wachler in 2004.
- A few peer reviewed articles in medical literature.

Questions/concerns raised by Seiler and others:
- Can enough riboflavin penetrate into the cornea?
- Danger to endothelium & macula if too much UV enters the eye
- Research: After 30 minutes:
  - Insufficient riboflavin concentration in the corneal stroma with Epi-On?
  - Does the Epithelium absorb too much UV:
    - This would diminish the effect of CXL?

Advantages of Epi-ON CXL

- Faster visual recovery:
  - Return to contact lenses in days
- Less pain
- Avoids risk of delays in epithelial healing
- Reduced risk of infection
- Reduced development of corneal haze

Keys to Trans-epithelial CXL

- Riboflavin 1% with gum cellulose Q2 min:
  - From local compounding pharmacies.
- Topical Tetracaine with BAK provided Q2 to 5 min
- Corneal Protector sponge used
- 60-80 minutes of Riboflavin drops required

Indications:
- Keratoconus
- FFKC
- Pellucid
- Post-LASIK ectasia

Fluorescence Microscopy

3000ms Exposure time, 10x

| Riboflavin for 30 min, No UVA, with Epithelium |
| Riboflavin for 30 min, No UVA, no Epithelium |

Asota, Fant, Edelhauser, and Stulting, unpublished
Evaluation of Corneal Saturation: Epi-On

Transition between sufficient corneal saturation with riboflavin

Keys to Trans-epithelial CXL
- 30 min of UV light applied:
  - Once sufficient riboflavin present in the corneal stroma
  - Minimum of 400 micron pach required before UV light

Fluorescence of cornea with UV light

Optical Coherence Tomography

Questions
- Is it safe?
- Does it work?
- Who is a candidate?
- What is my role?

Safety
- Loss of Best Corrected Vision
- Endothelial Cell Loss
- Infection
- Haze

Evaluation of Studies BCVA
- Siena Eye Crosslinking Study
  - 44 Eyes followed 48 months
  - No loss of BCVA at 48 months
- Transepithelial Crosslinking Study
  - 55 Eyes followed 24 months
  - 1 patient 1 line decrease BCVA
  - 0 patients 2 line decrease BCVA
Safety of corneal collagen cross-linking with UV-A and riboflavin in progressive keratoconus.

- No change in endothelial cell thickness at 6 months and 12 months
- No change in foveal thickness at 6 months and 12 months


Permanent Stromal Haze after Crosslinking

- 163 Eyes of 127 patients treated with Riboflavin and UV light (370nm)
- At 1 year 8.6% developed permanent stromal haze
- Study compared the clear group to haze group

Raiskup F. Permanent stromal haze after Riboflavin UV Crosslinking in Keratoconus. JRS; Sept 2009.

Haze after CXL

- Differences in Haze Group

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>22</th>
</tr>
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<tbody>
<tr>
<td>Mean follow-up</td>
<td>23.2 ± 12.9 mos</td>
</tr>
<tr>
<td>Preoperative K progression</td>
<td>1.42 ± 1.18 D</td>
</tr>
<tr>
<td>Postoperative K regression</td>
<td>2.61 ± 1.74 0.0001</td>
</tr>
<tr>
<td>Postoperative regression in SE</td>
<td>1.14 ± 2.18 D 0.030</td>
</tr>
<tr>
<td>Postoperative increase in VA</td>
<td>1.26 ± 1.5 lines 0.026</td>
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</tbody>
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Cross-Linking and Keratoconus Keratometry Over Time

How Effective is CXL in this case?

Preop

Postop 3 M

2.8 D

Steeper

3.8 D

Flatter

William Trattler, MD

Epi-ON case

Topographic Symmetry

Prospective Randomized Trial Design: Australia

- Christine Wittig, Grant Snibson, Mark Whiting, Laurie Sullivan, Richard Lindsay, Hugh Taylor
- Melbourne, Brisbane
- Inclusion criteria
  - Keratoconus
  - Documented progression over 12 mo.
  - CT > 400 μ
  - Age 16-50
  - No corneal surgery or other pathology
  - Cross-over at 6 months if progression in control eyes

Prospective Randomized Trial Interim Results

- 66 eyes randomized
- Mean age 27.6 y

Prospective Randomized Trial Treatment Parameters

- Removal of epithelium
- Riboflavin drops q3 min x 15 min
- UVA with riboflavin q3 min
- Postoperative
  - TBL
  - Choramphenicol until ED healed
  - FML x 2 wk
**Prospective Randomized Trial**

K\(_{\text{max}}\) and K\(_{\text{min}}\)

**Best Corrected Vision**

**Long-term Results of Riboflavin UV A**

A Corneal Crosslinking for Keratoconus in Italy

Aldo Caporossi, MD

Cosimo Mazzatta, MD

American Journal of Ophthalmology

*Volume 149, Issue 4, Pages 585-593 (April 2010)*

**Methods**

- 44 Eyes with progressive keratoconus
- Mean K less than 55
- Greater than 400 microns thickness
- Cornea clear without scars

**Corneal Thickness**

**Keratometry**
Comparison of Sequential vs Same-day Simultaneous Collagen Cross-linking and Topography-guided PRK for Treatment of Keratoconus

Anastasios John Kanellopoulos, MD

Results

- BCVA improved 0.39 logmar to 0.11
- 3.2 Diopter reduction in SE
- 3.5D Flatten of mean K’s

Patient data and treatment

- 325 Keratoconus eyes
- Topography guided custom PRK
- CXL with riboflavin and UV light
- Maximum treatment 50 microns
- Treated 70% of cyl
What is the best parameter to measure success of CXL

1. Best Corrected Vision
2. Topographic Changes (I/S Ratio)
3. Change in Higher Order Aberrations
4. Patient Satisfaction Survey
5. Percentage of Soft Toric Wearers

Conclusions: CXL

- Halts progression of ectatic corneal diseases
- Decreases corneal curvature and thickness
- Regularizes corneal surface
- Improves UCVA and BSCVA
- Effect lasts indefinitely
- Offers safe and effective treatment for conditions with no currently available treatment and may avoid
  - 15% of corneal transplants
  - Disability, cost, loss of productivity, CTL

Indications for Intacs in Keratoconus or Post-Lasik Ectasia

- Patients are contact lens intolerant
- Are considering a cornea transplant
- Clear central cornea with no scar
- CL Visual acuity limits lifestyle
- Corneal thickness adequate at the site of proposed placement of segments

Contra-indications for Intacs

- Cornea with central scars and opacities
- Cornea too thin at the site of the Intacs implantation
- Patients with unrealistic expectations

Intacs with Sequential CXL

- Effects of both treatments are synergistic
  - Increased K flattening
  - Increased BCVA
  - Increased UCVA

Edema Post CXL / Intacs

Shapes
- Standard
- Top Hat
- Mushroom
- Zig Zag
- Christmas Tree
- Zig Square

Transition to Refractive Suite
- Just beginning
  - Interrupted cuts to preserve globe integrity
  - Donor tissue preparation
    - Collaboration with eye banks
- Practical Mechanics
  - 100-400 um gap
  - Horizontal orientation allows blunt dissection
  - Vertical overlap on posterior side cut to ensure intersection

Top Hat Shaped Keratoplasty
- For endothelial disease
- Provides large endothelial surface transplantation

Mushroom Shaped Keratoplasty
- For anterior corneal disease
- Preserves more host endothelium

Zig-Zag Shaped Keratoplasty
- Hermetic wound seal
- Angled edge provides smooth transition between host and donor
Zig-Zag Shaped Keratoplasty

The Zig-Zag shaped incision creates a smooth corneal contour immediately after surgery with less distortion of the corneal optics and less astigmatism.

Image courtesy of Roger F. Steinert, MD
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IntraLase Advanced Keratoplasty

1 month OCT. The Zig-Zag shaped incision creates a smooth corneal contour immediately after surgery with less distortion of the corneal optics and less astigmatism.

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Zig-Zag Shaped Keratoplasty

The Zig-Zag shaped incision is more prominent at 3 months, suggesting early fibrosis.

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Not all keratoconus is the same

Case Study

- 38 y/o male
- OD – 3.00-1.25x135 20/25
- Soft toric never aligns to stable location
- Patient does not like comfort of RGP
- Vision with RGP 20/20-
Topography

What is your recommended treatment?
1. SynergEyes
2. CXL
3. Intacs
4. CXL and Intacs
5. PRK

Post – Op 10 years later

Keratoconus Progression
- Early Keratoconus – Moves from Soft toric to RGP Lenses
- Advancing Keratoconus – RGP lenses to specialty RGP / Hybrid Lenses
  - Consider CXL / Intacs
- Advanced Keratoconus – Decreased wearing time
  - Intacs if stable
  - Intacs and CXL if not stable

Thank You